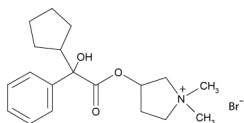


## BENZTROPINE MESYLATE - bentropine mesylate tablet

Rising Pharmaceuticals Inc

**DESCRIPTION:** Bentropine mesylate is a synthetic compound containing structural features found in atropine and diphenhydramine.

It is a crystalline white powder, very soluble in water. It is designated chemically as 3 $\alpha$ -(Diphenylmethoxy)-1 $\alpha$ H, 5 $\alpha$ H-tropane methanesulfonate. Its molecular formula is C<sub>21</sub>H<sub>25</sub>NO • CH<sub>4</sub>O<sub>3</sub>S, and its structural formula is:



Each tablet, for oral administration, contains 0.5 mg, 1 mg, or 2 mg of bentropine mesylate. Each tablet contains the following inactive ingredients: magnesium stearate, microcrystalline cellulose, povidone and pregelatinized starch.

**CLINICAL PHARMACOLOGY:** Bentropine possesses both anticholinergic and antihistaminic effects, although only the former have been established as therapeutically significant in the management of parkinsonism.

In the isolated guinea pig ileum, the anticholinergic activity of this drug is about equal to that of atropine; however, when administered orally to unanesthetized cats, it is only about half as active as atropine.

In laboratory animals, its antihistaminic activity and duration of action approach those of pyrilamine maleate.

**INDICATIONS AND USAGE:** For use as an adjunct in the therapy of all forms of parkinsonism.

Useful also in the control of extrapyramidal disorders (except tardive dyskinesia - see **PRECAUTIONS**) due to neuroleptic drugs (e.g., phenothiazines).

**CONTRAINDICATIONS:** Hypersensitivity to bentropine mesylate tablets.

Because of its atropine-like side effects, this drug is contraindicated in pediatric patients under three years of age and should be used with caution in older pediatric patients.

**WARNINGS:** Safe use in pregnancy has not been established.

Bentropine mesylate may impair mental and/or physical abilities required for performance of hazardous tasks such as operating machinery or driving a motor vehicle.

When bentropine is given concomitantly with phenothiazines, haloperidol, or other drugs with anticholinergic or antidopaminergic activity, patients should be advised to report gastrointestinal complaints, fever or heat intolerance promptly. Paralytic ileus, hyperthermia and heat stroke, all of which have sometimes been fatal, have occurred in patients taking anticholinergic-type antiparkinsonism drugs, including bentropine in combination with phenothiazines and/or tricyclic antidepressants.

Since bentropine contains structural features of atropine, it may produce anhidrosis. For this reason, it should be administered with caution during hot weather, especially when given concomitantly with other atropine-like drugs to the chronically ill, the alcoholic, those who have central nervous system disease, and those who do manual labor in a hot environment. Anhidrosis may occur more readily when some disturbance of sweating already exists. If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased at the discretion of the physician so that the ability to maintain body heat equilibrium by perspiration is not impaired. Severe anhidrosis and fatal hyperthermia have occurred.

### **PRECAUTIONS:**

#### *General*

Since bentropine mesylate has cumulative action, continued supervision is advisable. Patients with a tendency to tachycardia and patients with prostatic hypertrophy should be observed closely during treatment.

Dysuria may occur, but rarely becomes a problem. Urinary retention has been reported with bentropine.

The drug may cause complaints of weakness and inability to move particular muscle groups, especially in large doses. For example, if the neck has been rigid and suddenly relaxes, it may feel weak, causing some concern. In this event dosage adjustment is required.

Mental confusion and excitement may occur with large doses, or in susceptible patients. Visual hallucinations have been reported occasionally. Furthermore, in the treatment of extrapyramidal disorders due to neuroleptic drugs (e.g., phenothiazines) in patients with mental disorders, occasionally there may be intensification of mental symptoms. In such cases, antiparkinsonian drugs can precipitate a toxic psychosis. Patients with mental disorders should be kept under careful observation, especially at the beginning of treatment or if dosage is increased.

Tardive dyskinesia may appear in some patients on long-term therapy with phenothiazines and related agents or may occur after therapy with these drugs has been discontinued. Antiparkinsonism agents do not alleviate the symptoms of tardive dyskinesia, and in some instances may aggravate them. Bentropine is not recommended for use in patients with tardive dyskinesia.

The physician should be aware of the possible occurrence of glaucoma. Although the drug does not appear to have any adverse effect on simple glaucoma, it probably should not be used in angle-closure glaucoma.

#### *Drug Interactions*

Antipsychotic drugs such as phenothiazines or haloperidol; tricyclic antidepressants (see **WARNINGS**).

#### *Pediatric Use:*

Because of the atropine-like side effects, benztropine mesylate should be used with caution in pediatric patients over three years of age (see **CONTRAINDICATIONS** ).

**ADVERSE REACTIONS:** The adverse reactions below, most of which are anticholinergic in nature, have been reported and within each category are listed in order of decreasing severity.

*Cardiovascular:*

Tachycardia.

*Digestive:*

Paralytic ileus, constipation, vomiting, nausea, dry mouth.

If dry mouth is so severe that there is difficulty in swallowing or speaking, or loss of appetite and weight, reduce dosage, or discontinue the drug temporarily.

Slight reduction in dosage may control nausea and still give sufficient relief of symptoms. Vomiting may be controlled by temporary discontinuation, followed by resumption at a lower dosage.

*Nervous System:*

Toxic psychosis, including confusion, disorientation, memory impairment, visual hallucinations; exacerbation of pre-existing psychotic symptoms; nervousness; depression; listlessness; numbness of fingers.

*Special Senses:*

Blurred vision, dilated pupils.

*Urogenital:*

Urinary retention, dysuria.

*Metabolic/Immune or Skin:*

Occasionally, an allergic reaction, e.g., skin rash, develops. If this can not be controlled by dosage reduction, the medication should be discontinued.

*Other:*

Heat stroke, hyperthermia, fever.

**OVERDOSAGE:**

*Manifestations* — May be any of those seen in atropine poisoning or antihistamine overdosage: CNS depression, preceded or followed by stimulation; confusion; nervousness; listlessness; intensification of mental symptoms or toxic psychosis in patients with mental illness being treated with

neuroleptic drugs (e.g., phenothiazines); hallucinations (especially visual); dizziness; muscle weakness; ataxia; dry mouth; mydriasis; blurred vision; palpitations; tachycardia; elevated blood pressure; nausea; vomiting; dysuria; numbness of fingers; dysphagia; allergic reactions, e.g., skin rash; headache; hot, dry, flushed skin; delirium; coma; shock; convulsions; respiratory arrest; anhidrosis; hyperthermia; glaucoma; constipation.

*Treatment* — Physostigmine salicylate, 1 to 2 mg, sc or iv, reportedly will reverse symptoms of anticholinergic intoxication<sup>1</sup>. A second injection may be given after 2 hours if required. Otherwise treatment is symptomatic and supportive. Induce emesis or perform gastric lavage (contraindicated in precoma, convulsive, or psychotic states). Maintain respiration. A short-acting barbiturate may be used for CNS excitement, but with caution to avoid subsequent depression; supportive care for depression (avoid convulsant stimulants such as picrotoxin, pentylenetetrazol, or bemegride); artificial respiration for severe respiratory depression; a local miotic for mydriasis and cycloplegia; ice bags or other cold applications and alcohol sponges for hyperpyrexia, a vasopressor and fluids for circulatory collapse. Darken room for photophobia.

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1Duvoisin, R.C.; Katz, R.J.; Amer. Med. Ass. 206: 1963-1965, Nov. 25, 1968.

**DOSAGE AND ADMINISTRATION:** Benzotropine mesylate tablets should be used when patients are able to take oral medication. The injection is especially useful for psychotic patients with acute dystonic reactions or other reactions that make oral medication difficult or impossible. It is recommended also when a more rapid response is desired than can be obtained with tablets.

Because of cumulative action, therapy should be initiated with a low dose which is increased gradually at five or six-day intervals to the smallest amount necessary for optimal relief. Increases should be made in increments of 0.5 mg to a maximum of 6 mg or until optimal results are obtained without excessive adverse reactions.

*Postencephalitic and Idiopathic Parkinsonism* — The usual daily dose is 1 to 2 mg with a range of 0.5 to 6 mg orally or parenterally. As with any agent used in parkinsonism, dosage must be individualized according to age and weight, and the type of parkinsonism being treated. Generally, older patients, and thin patients cannot tolerate large doses. Most patients with postencephalitic parkinsonism need fairly large doses and tolerate them well. Patients with a poor mental outlook are usually poor candidates for therapy.

In idiopathic parkinsonism, therapy may be initiated with a single daily dose of 0.5 to 1 mg at bedtime. In some patients, this will be adequate; in others 4 to 6 mg a day may be required. In postencephalitic parkinsonism, therapy may be initiated in most patients with 2 mg a day in one or more doses. In highly sensitive patients, therapy may be initiated with 0.5 mg at bedtime, and increased as necessary.

Some patients experience greatest relief by taking the entire dose at bedtime, others react more favorably to divided doses, two to four times a day. Frequently, one dose a day is sufficient and divided doses may be unnecessary or undesirable.

The long duration of action of this drug makes it particularly suitable for bedtime medication when its effects may last throughout the night, enabling patients to turn in bed during the night more easily, and to rise in the morning.

When benzotropine is started, do not terminate therapy with other antiparkinsonian agents abruptly. If the other agents are to be reduced or discontinued, it must be done gradually. Many patients obtain greatest relief with combination therapy.

Benzotropine mesylate may be used concomitantly with carbidopa-levodopa, or with levodopa, in which case periodic dosage adjustment may be required in order to maintain optimum response.

**Drug-Induced Extrapyramidal Disorders**— In treating extrapyramidal disorders due to neuroleptic drugs (e.g., phenothiazines), the recommended dosage is 1 to 4 mg once or twice a day orally or parenterally. Dosage must be individualized according to the need of the patient. Some patients require more than recommended; others do not need as much.

When extrapyramidal disorders develop soon after initiation of treatment with neuroleptic drugs (e.g., phenothiazines), they are likely to be transient. One to 2 mg of benzotropine mesylate tablets two or three times a day usually provides relief within one or two days. After one or two weeks, the drug should be withdrawn to determine the continued need for it. If such disorders recur, benzotropine mesylate can be reinstituted.

Certain drug-induced extrapyramidal disorders that develop slowly may not respond to benzotropine.

**HOW SUPPLIED:** Benzotropine mesylate tablets USP 0.5 mg - Each white, round compressed tablet is scored and debossed with identification logo cor and 143 on one side.

NDC 64980-111-01 in bottles of 100 tablets

NDC 64980-111-10 in bottles of 1000 tablets

Benzotropine mesylate tablets USP 1 mg - Each white, oval shaped compressed tablet is scored and debossed with identification logo cor and 144 on one side.

NDC 64980-112-01 in bottles of 100 tablets

NDC 64980-112-10 in bottles of 1000 tablets

Benzotropine mesylate tablets USP 2 mg - Each white, round compressed tablet is scored and debossed with identification logo cor and 145 on one side.

NDC 64980-113-01 in bottles of 100 tablets

NDC 64980-113-10 in bottles of 1000 tablets

Store at controlled room temperature 15° - 30°C (59° - 86°F) (see USP).

Dispense in well-closed container as defined in the USP.

Manufactured by:

Corepharma LLC

Middlesex, NJ 08846

MF # 276-03



Manufactured for:

Rising Pharmaceuticals, Inc.

Allendale, NJ 07401

Rev. July 2009

**Rising** NDC 64980-111-01

**Benzotropine Mesylate Tablets USP**  
0.5 mg  
Rx Only  
100 Tablets

Each tablet contains 0.5 mg of benzotropine mesylate USP, a centrally acting anticholinergic drug. Usual Adult Dosage: For parkinsonism, 1 mg orally 3 to 4 times daily. For drug-induced extrapyramidal disorders, 1 to 4 mg orally 3 to 4 times daily. See package insert for complete prescribing information.

Store at controlled room temperature 15° - 30°C (59° - 86°F) (see USP). Dispense in well-closed container as defined in the USP.

Keep this and all drugs out of the reach of children. See package insert for complete prescribing information.

Manufactured for:  
Corepharma LLC  
Middlesex, NJ 08846  
MF # 264-02

Rev. 01-2007

**CorePharma LLC**

Lot No: 3 64980-111-01 0  
Exp. Date:

**Rising** NDC 64980-112-01

**Benzotropine Mesylate Tablets USP**  
1 mg  
Rx Only  
100 Tablets

Each tablet contains 1 mg of benzotropine mesylate USP, a centrally acting anticholinergic drug. Usual Adult Dosage: For parkinsonism, 1 mg orally 3 to 4 times daily. For drug-induced extrapyramidal disorders, 1 to 4 mg orally 3 to 4 times daily. See package insert for complete prescribing information.

Store at controlled room temperature 15° - 30°C (59° - 86°F) (see USP). Dispense in well-closed container as defined in the USP.

Keep this and all drugs out of the reach of children. See package insert for complete prescribing information.

Manufactured for:  
Corepharma LLC  
Middlesex, NJ 08846  
MF # 267-02

Rev. 01-2007

**CorePharma LLC**

Lot No: 3 64980-112-01 7  
Exp. Date:

**Rising** NDC 64980-113-01

**Benzotropine Mesylate Tablets USP**  
2 mg  
Rx Only  
100 Tablets

Each tablet contains 2 mg of benzotropine mesylate USP, a centrally acting anticholinergic drug. Usual Adult Dosage: For parkinsonism, 1 mg orally 3 to 4 times daily. For drug-induced extrapyramidal disorders, 1 to 4 mg orally 3 to 4 times daily. See package insert for complete prescribing information.

Store at controlled room temperature 15° - 30°C (59° - 86°F) (see USP). Dispense in well-closed container as defined in the USP.

Keep this and all drugs out of the reach of children. See package insert for complete prescribing information.

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MF # 271-02

Rev. 01-2007

**CorePharma LLC**

Lot No: 3 64980-113-01 4  
Exp. Date: